

Contents lists available at [ScienceDirect](http://ScienceDirect.com)

Journal of Cardiology

journal homepage: www.elsevier.com/locate/jjcc

Editorial

Intravascular ultrasound-derived tissue characterization of the in-stent neointima: Are they “true colors” shining through?



Intravascular ultrasound (IVUS) has been developed as a novel gray scale imaging of the coronary vessel wall in vivo. IVUS-based cross-sectional imaging provides additional information, such as vessel, lumen, and plaque area and thus helps the undertaking of percutaneous coronary intervention more effectively and safely. In addition to the quantitative assessment, visual interpretations of the gray scale IVUS image may help in assessing plaque as well as neointimal characteristics. Despite the fact that we can assess plaque vulnerability as well as risk for slow flow/no reflow during PCI [1,2], gray scale IVUS-derived tissue qualitative assessment may not be enough because of its subjective and less quantitative nature.

Three different IVUS-based tissue characterization algorithms based on radio frequency signal processing have been developed to provide more objective and quantitative information of the coronary plaque in vivo [3–5]. One of the tissue characterizations is virtual histology intravascular ultrasound (VH-IVUS) [3]. VH-IVUS-based tissue characterization has been reported as useful to predict coronary microembolization during percutaneous coronary intervention [3] and future coronary events [6]. The second tissue characterization technique is an integrated backscatter (IB)-IVUS [5,7–9]. Similar to the VH-IVUS, IB-IVUS may be useful to detect unstable or vulnerable plaque [5] and future coronary events [8]. Although these tissue characterization systems have been validated to assess coronary plaque by comparing with histology [7], IB-IVUS may have some role in the assessment of intrastent neointimal tissue characterization [10]. In fact, IVUS has been used to quantitate in-stent neointimal hyperplasia [11]. Therefore, use of tissue characterization may have an additional role in volumetric neointimal analysis using gray scale IVUS alone. In this issue of the journal, Araki and co-workers [12], by using another IVUS-based tissue characterization system [12], iMap [9,13], reported that in-stent neointimal tissue components may be different between early and late drug-eluting stent restenosis. The iMap has been developed as the third IVUS-based tissue characterization system [9,13]. The iMap classifies tissue components into four categories: fibrotic, lipidic, necrotic, and calcified [13]. Although iMap has not been developed to assess in-stent neointima but to assess atherosclerotic coronary plaque, it may be possible to clarify the differences in the in-stent neointimal tissue components. In fact, in-stent neointimal tissue components

classified by iMap were different between early (<1 year) and late (>1 year) in-stent stenoses. This is in agreement with a previous study using optical coherence tomography showing that late in-stent restenosis after drug-eluting stent implantation may have neoatherosclerosis [14]. Because IVUS has an advantage over optical coherence tomography with respect to the assessment of entire vessel structure [15], iMap-based tissue characterization may have some clinical implications.

Although the results of this manuscript are interesting, several limitations should be addressed. First, iMap-derived tissue characterization is not compatible with other tissue characterization techniques because of differences in the signal processing algorithm [9]. Therefore, these results should be carefully interpreted. Similarly, because iMap does not have histological validation for in-stent neointimal tissue, the iMap findings need to be confirmed by histological examination. Finally, the impact of iMap findings of in-stent neointimal tissue on future events or risk of slow flow/no reflow during percutaneous coronary intervention is uncertain. Color-coded IVUS images are beautiful as if they are providing “true colors” of the in-stent neointimal tissue characteristics. However, until the above issues are addressed, these colors should be interpreted as virtual rather than true colors.

References

- [1] Okura H, Taguchi H, Kubo T, Toda I, Yoshida K, Yoshiyama M, Yoshikawa J. Atherosclerotic plaque with ultrasonic attenuation affects coronary reflow and infarct size in patients with acute coronary syndrome: an intravascular ultrasound study. *Circ J* 2007;71:648–53.
- [2] Yamada R, Okura H, Kume T, Neishi Y, Kawamoto T, Watanabe N, Toyota E, Yoshida K. Histological characteristics of plaque with ultrasonic attenuation: a comparison between intravascular ultrasound and histology. *J Cardiol* 2007;50:223–8.
- [3] Kawamoto T, Okura H, Koyama Y, Toda I, Taguchi H, Tamita K, Yamamoto A, Yoshimura Y, Neishi Y, Toyota E, Yoshida K. The relationship between coronary plaque characteristics and small embolic particles during coronary stent implantation. *J Am Coll Cardiol* 2007;50:1635–40.
- [4] Yamada R, Okura H, Kume T, Neishi Y, Kawamoto T, Miyamoto Y, Imai K, Saito K, Tsuchiya T, Hayashida A, Yoshida K. Target lesion thin-cap fibroatheroma defined by virtual histology intravascular ultrasound affects microvascular injury during percutaneous coronary intervention in patients with angina pectoris. *Circ J* 2010;74:1658–62.
- [5] Miyamoto Y, Okura H, Kume T, Kawamoto T, Neishi Y, Hayashida A, Yamada R, Imai K, Saito K, Yoshida K. Plaque characteristics of thin-cap fibroatheroma evaluated by OCT and IVUS. *JACC Cardiovasc Imaging* 2011;4:638–46.
- [6] Stone GW, Maehara A, Lansky AJ, de Bruyne B, Cristea E, Mintz GS, Mehran R, McPherson J, Farhat N, Marso SP, Parise H, Templin B, White R, Zhang Z, Serruys PW, et al. A prospective natural-history study of coronary atherosclerosis. *N Engl J Med* 2011;364:226–35.
- [7] Kawasaki M, Takatsu H, Noda T, Sano K, Ito Y, Hayakawa K, Tsuchiya K, Arai M, Nishigaki K, Takemura G, Minatoguchi S, Fujiwara T, Fujiwara H. In vivo

DOI of original article: <http://dx.doi.org/10.1016/j.jjcc.2014.03.001><http://dx.doi.org/10.1016/j.jjcc.2014.05.002>

0914-5087/© 2014 Japanese College of Cardiology. Published by Elsevier Ltd. All rights reserved.

- quantitative tissue characterization of human coronary arterial plaques by use of integrated backscatter intravascular ultrasound and comparison with angioscopic findings. *Circulation* 2002;105:2487–92.
- [8] Sano K, Kawasaki M, Ishihara Y, Okubo M, Tsuchiya K, Nishigaki K, Zhou X, Minatoguchi S, Fujita H, Fujiwara H. Assessment of vulnerable plaques causing acute coronary syndrome using integrated backscatter intravascular ultrasound. *J Am Coll Cardiol* 2006;47:734–41.
- [9] Yamada R, Okura H, Kume T, Neishi Y, Kawamoto T, Miyamoto Y, Imai K, Saito K, Hayashida A, Yoshida K. A comparison between 40 MHz intravascular ultrasound iMap imaging system and integrated backscatter intravascular ultrasound. *J Cardiol* 2013;61:149–54.
- [10] Muraoka Y, Sonoda S, Kashiya K, Kamezaki F, Tsuda Y, Araki M, Okazaki M, Otsuji Y. Evaluation of in-stent neointimal tissue components using integrated backscatter intravascular ultrasound: comparison of drug-eluting stents and bare-metal stents. *Int J Cardiovasc Imaging* 2012;28:1635–41.
- [11] Takagi T, Okura H, Kobayashi Y, Kataoka T, Taguchi H, Toda I, Tamita K, Yamamuro A, Sakanoue Y, Ito A, Yanagi S, Shimeno K, Waseda K, Yamasaki M, Fitzgerald PJ, et al. A prospective, multicenter, randomized trial to assess efficacy of pioglitazone on in-stent neointimal suppression in type 2 diabetes: POPPS (Prevention of In-Stent Neointimal Proliferation by Pioglitazone Study). *JACC Cardiovasc Interv* 2009;2:524–31.
- [12] Araki T, Nakamura M, Sugi K. Characterization of in-stent neointimal tissue components following drug-eluting stent implantation according to the phase of restenosis using a 40-MHz intravascular ultrasound imaging system. *J Cardiol* 2014;64:423–9.
- [13] Sathyanarayana S, Carlier S, Li W, Thomas L. Characterisation of atherosclerotic plaque by spectral similarity of radiofrequency intravascular ultrasound signals. *EuroIntervention* 2009;5:133–9.
- [14] Kang SJ, Mintz GS, Akasaka T, Park DW, Lee JY, Kim WJ, Lee SW, Kim YH, Whan Lee C, Park SW, Park SJ. Optical coherence tomographic analysis of in-stent neoatherosclerosis after drug-eluting stent implantation. *Circulation* 2011;123:2954–63.
- [15] Yamada R, Okura H, Kume T, Saito K, Miyamoto Y, Imai K, Tsuchiya T, Maehama T, Okahashi N, Obase K, Hayashida A, Neishi Y, Kawamoto T, Yoshida K. Relationship between arterial and fibrous cap remodeling: a serial three-vessel intravascular ultrasound and optical coherence tomography study. *Circ Cardiovasc Interv* 2010;3:484–90.

Hiroiyuki Okura (MD)*

*Division of Cardiology, Kawasaki Medical School, 577 Matsushima
Kurashiki, Okayama 701-0192, Japan*

*Tel.: +81 086 462 1111; fax: +81 086 462 1199

E-mail address: hokura@fides.dti.ne.jp (H. Okura).

1 May 2014

Available online 18 September 2014